

Overcoming perceptions of financial barriers to rotavirus vaccine introduction in Asia

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Abbreviations: ACIP, Advisory Committee on Immunization Practices; ARSN, Asian Rotavirus Surveillance Network; ATAGI, Australian Technical Advisory Group on Immunization; GAVI, GAVI Alliance; ICER, incremental cost-effective ratio; NIP, National Immunization Program; NITAG, national immunization technical advisory committees; PAHO, Pan American Health Organization; PBAC, Pharmaceutical Benefits Advisory Committee; SAGE, Strategic Advisory Group of Experts; WHO, World Health Organization

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Overview

Despite a WHO recommendation in 2009, reaffirmed in 2013, that all countries should consider introducing rotavirus vaccines into their National Immunization Programs, as of June 2013 only 45 have done so. One major consideration appears to have been the costs of the vaccine to countries. Of concern is that Asian countries have been slow to introduce rotavirus vaccines despite having robust data that could inform the decision-making process. Although decisions on new vaccine introduction are very complex and vary by country and region, economic evaluations are often pivotal once vaccine efficacy and safety has been established, and disease burden documented and communicated. Unfortunately, with private sector list prices of vaccines often used in economic evaluations, rather than a potential public health sector pricing structure, policy-makers may defer decisions on rotavirus vaccine introduction based on the belief that “the vaccine price is too high,” even though this might be based on erroneous data. The Pan American Health Organization’s Revolving Fund provides one example of how vaccine price can be made more competitive and transparent through a regional tendering process. Other mechanisms, such as tiered pricing and UNICEF procurement, also exist that could help Asian and other countries move forward more quickly with rotavirus vaccine introduction.

The first rotavirus vaccine, Rotashield®, was licensed by the United States Food and Drug Administration (FDA) and recommended for universal use in the United States in 1998. Post-marketing surveillance identified that the vaccine was associated with an increased risk of intussusception of approximately 1 in 10 000 vaccinated infants and it was voluntarily withdrawn from the United States market by the manufacturer in 1999. In January 2006, results of two large clinical trials of two new rotavirus vaccines, Rotarix® and RotaTeq®, each with over 60 000 infants for safety, reported good safety and high efficacy against severe rotavirus gastroenteritis during the first two years of life.^{1,2} These vaccines showed no increased risk of intussusception in the infants, although cases were identified in both vaccine and placebo recipients. Following the 2007 World Health Organization (WHO) recommendation to introduce rotavirus vaccines in the regions where vaccine efficacy had been demonstrated in initial clinical trials (the Americas and Europe),³ many countries in these regions implemented rotavirus vaccination in their national programs over the next few years (Table 1). After clinical trials in Africa and Asia were completed, WHO expanded its initial recommendation in 2009 and recommended introduction of rotavirus vaccination in all countries in the world.⁴

The early adopter countries have witnessed substantial reductions in rotavirus-associated hospitalization rates

in children under two-years of age in high income countries (Australia,^{5,6} Austria,⁷ Belgium,^{8,9} United States¹⁰) and middle- or low-income countries (Brazil,^{11,12} El Salvador,^{13,14} Mexico,¹⁵ Nicaragua,¹⁶ Panama,¹⁷). Overall, where reported, rotavirus hospitalizations have fallen by around 70% and all-cause gastroenteritis hospitalizations by around 35% (Table 1).¹⁸ In addition universal rotavirus vaccination may have reduced nosocomial infections,¹⁹ and has been documented to provide significant indirect protection to unvaccinated older children and adults.²⁰ Finally, it is most exciting to note that substantial 30–40% declines in diarrhea mortality, an outcome not assessed in rotavirus vaccine clinical trials, have been noted in two large middle-income countries in Latin America (Mexico and Brazil) that have examined national data on diarrhea deaths in children.^{12,21}

In January 2013, the WHO updated its previous position papers on rotavirus vaccines and reaffirmed its 2009 recommendation that rotavirus vaccines should be included in all National Immunization Programs (NIPs) globally.²² Yet as of June 2013, only 45 countries have followed this advice, with an additional 3 countries recommending the vaccine for sub-national introduction (Table 1). Why did some countries recommend vaccine introduction within months of licensure, while others have not?

Factors Influencing Decision-Making Regarding New Vaccine Introduction

In 2002, McKinsey and Co. reported to the GAVI Alliance (GAVI) on factors that decision-makers indicated could accelerate the decision for introduction of new vaccines in developing countries. These included (1) proof of local disease burden, (2) proof of an available safe and effective vaccine, and (3) evidence of value for money. Other factors influencing the decision-making process included the potential impact on existing immunization programs and support for the new vaccine from clinical opinion leaders, medical practitioners and the general public. In 2007 McKinsey and Co. undertook a pro-bono “Network Analysis” liaising with the Bill and Melinda Gates Foundation, John

Hopkins Bloomberg School of Public Health, the PneumoADIP and PATH.²³ This analysis focused on four countries (Egypt, Mauritania, Mexico, Zambia) and mapped the complex relationships between the influencers of the decision making process. Although international organizations were shown to play a key role in the introduction process, there was seen to be a failure to utilize global experts and little cross-country sharing of information. Improving connectivity at an early stage, with involvements of Ministries of Finance and community groups, were suggested as key influencing factors. In addition a perceived lack of data on local disease burden was highlighted as an important barrier to introduction decisions. However, a perception of lack data on disease burden may reflect a failure to communicate these data to both national decision-makers and the general public, rather than a deficiency of scientific evidence. More recently, a study looking at new vaccine introductions in lower-middle-income countries has highlighted that disease burden, cost and WHO recommendations remain key influencers to the decision making process.²⁴

We examine the availability of evidence for these key factors to support decision making for countries in Asia, and look at how financial barriers may play a major role in the lack of uptake of rotavirus vaccines. Additional factors play a role in the decision-making process, such as percentage of national budget allocated to health, real and perceived health priorities, arguments that new vaccine introductions should be sequential and competitive, and public knowledge of and demand for a vaccine are not directly considered.

Disease Burden of Rotavirus in Asia

To accelerate the introduction of rotavirus vaccines WHO and GAVI recognized early the importance of collecting local disease burden data for policy makers and recommended that simple generic protocols be developed and that regional rotavirus surveillance networks be established.²⁵ The first such network to be established was the Asian Rotavirus Surveillance Network (ARSN) which used a WHO active surveillance

protocol.²⁶ The initial phase conducted standardized surveillance in China, Hong Kong, Indonesia, Malaysia, Myanmar, South Korea, Taiwan, Thailand, and Vietnam between 2001–2004, followed by a second phase between 2005–2007 in predominantly GAVI-eligible countries (Table 2).²⁵ The extensive data collected by the ARSN were widely published and made available for decision makers in the region. The ARSN data included disease burden estimates from some of the world’s most populous countries (China, India, Indonesia, Pakistan, and Bangladesh) and shows that for a number of countries over 50% of gastroenteritis-related hospital admissions were due to rotavirus (Table 2).^{26,27} Yet as of June 2013 only two countries in the Asian region, Philippines and Thailand, had partially introduced rotavirus vaccines into their immunization programs. This experience suggests that having an extensive database of local disease burden alone has been insufficient to drive rapid introduction of rotavirus vaccine in the Asian region.

Rotavirus Vaccine Efficacy in Asia

Rotavirus vaccine efficacy trials in Asia lagged behind those in the Americas and Europe by several years and initially involved only high income countries in the region (Hong Kong, Singapore, and Taiwan).²⁸ This study demonstrated vaccine efficacy of 96.1% (95% CI: 85.1%; 99.5%) against severe rotavirus gastroenteritis during the first two years of life, with sustained efficacy of 100% (95% CI: 67.5%; 100%) in the third-year.²⁹ Efficacy studies in middle- and low-income countries in Asia followed several years later, demonstrating good efficacy in Vietnam and only modest efficacy in Bangladesh.³⁰ Thus, local evidence of vaccine performance from a variety of socioeconomic settings in Asia is also available, including the significant public health impact of vaccine in Bangladesh, even with a modest vaccine efficacy.⁴ The perception of a lack of “good” efficacy data in low income settings in the region, despite the WHO Strategic Advisory Group of Experts (SAGE) recommendation of significant public health impact in these populations,^{4,22}

Table 1. Countries by regions that have introduced rotavirus vaccine in their National Immunization Programs (NIPs) a,⁴⁷ as of June 2013 and subsequent reductions and rotavirus and all-cause gastroenteritis (GE)¹⁸

WHO region	Country	World Bank classification	Month and year of introduction	Vaccine	Reduction in rotavirus admission <2 y	Reduction in all-cause GE admission <2 y
Americas (PAHO) (19)	Brazil ^b	UMIC	2006	Rotarix [®]	59%	17–48%
	El Salvador ^b	LMIC	2006	Rotarix [®]		28–37%
	Nicaragua ^b	LMIC	2006	RotaTeq [®]		
	Panama ^b	UMIC	2006	Rotarix [®]		37%
	USA ^b	HIC	2006	RotaTeq [®] and later Rotarix [®]	66–86%	29–50%
	Venezuela ^b	UMIC	2006	Rotarix [®]		
	Ecuador ^b	UMIC	2007	Rotarix [®]		
	Mexico ^b	UMIC	2007	Rotarix [®]		40%
	Bolivia	LMIC	2008	Rotarix [®]		
	Cayman Islands ^c	HIC	2009	RotaTeq [®]		
	Colombia	UMIC	2009	Rotarix [®]		
	Honduras	LMIC	2009	Rotarix [®]		
	Paraguay	LMIC	2009	Rotarix [®]		
	Peru	UMIC	2009	Rotarix [®]		
	Guatemala	LMIC	2010	Rotarix [®]		
	Guyana	LMIC	2010	RotaTeq [®]		
	Canada (Ontario) ^d	HIC	2011	Rotarix [®]		
	Dominican Republic	UMIC	2012	Rotarix [®]		
	Haiti	LIC	2013	Rotarix [®]		
Europe (EURO) (8)	Austria ^b	HIC	2006	Rotarix [®]	74–79%	
	Luxembourg ^b	HIC	2006	Rotarix [®]		
	Belgium ^b	HIC	2007	Rotarix [®] and RotaTeq [®]	50–77%	33%
	Finland	HIC	2009	RotaTeq [®]		
	Israel	HIC	2010	RotaTeq [®]		
	Armenia	LMIC	2012	Rotarix [®]		
	Republic of Moldova	LMIC	2012	Rotarix [®]		
Western Pacific (WPRO) (6)	Georgia	LMIC	2013	Rotarix [®]		
	Australia ^b	HIC	2007	Rotarix [®] and RotaTeq [®]	87%	
	Palau	UMIC	2008	Rotarix [®]		
	Marshall Islands	LMIC	2009	RotaTeq [®]		

HIC, high income country; UMIC, upper middle income country—\$4036 to \$12 475 per capita gross national income (GNI); LMIC, lower middle income country—\$1026 to \$4035 GNI; LIC, low income country—\$1025 or less GNI. aThe PATH Rotavirus Vaccine Access and Delivery website has timely and useful maps and tools that provide the status of rotavirus vaccines introductions around the world. ^bEarly adopters (rotavirus vaccine introduced into during 2006/2007). cInformation from PAHO—not a WHO member state. ^dIntroduction to only part of the country. eIntroduction to National Immunization Program but initially only funds available to vaccinate an estimated 700 000 infants from the poorest communities.

Table 1. Countries by regions that have introduced rotavirus vaccine in their National Immunization Programs (NIPs) a,⁴⁷ as of June 2013 and subsequent reductions and rotavirus and all-cause gastroenteritis (GE)¹⁸ (continued)

WHO region	Country	World Bank classification	Month and year of introduction	Vaccine	Reduction in rotavirus admission <2 y	Reduction in all-cause GE admission <2 y
	Federated States of Micronesia	LMIC	2011	RotaTeq [®]		
	Fiji	LMIC	2012	Rotarix [®]		
	Philippines ^e	LMIC	2012	Rotarix [®]		
Eastern Mediterrean (EMRO) (7)	Bahrain	HIC	2008	Rotarix [®]		
	Qatar	HIC	2009	Rotarix [®]		
	Morocco	LMIC	2010	Rotarix [®]		
	Iraq	LMIC	2012	RotaTeq [®]		
	Yemen	LMIC	2012	Rotarix [®]		
	Saudi Arabia	HIC	2013	Rotarix [®]		
	Sudan	LMIC	2011	Rotarix [®]		
Africa (AFRO) (7)	South Africa	UMIC	2009	Rotarix [®]		
	Botswana	UMIC	2012	Rotarix [®]		
	Ghana	LMIC	2012	Rotarix [®]		
	Malawi	LIC	2012	Rotarix [®]		
	Rwanda	LIC	2012	RotaTeq [®]		
	Tanzania	LIC	2012	Rotarix [®]		
	Zambia ^d	LIC	2012	Rotarix [®]		
South East Asia (SEARO) (1)	Thailand ^d	UMIC	2012	Rotarix [®]		

HIC, high income country; UMIC, upper middle income country—\$4036 to \$12 475 per capita gross national income (GNI); LMIC, lower middle income country—\$1026 to \$4035 GNI; LIC, low income country—\$1025 or less GNI. aThe PATH Rotavirus Vaccine Access and Delivery website has timely and useful maps and tools that provide the status of rotavirus vaccines introductions around the world. ^bEarly adopters (rotavirus vaccine introduced into during 2006/2007). cInformation from PAHO—not a WHO member state. ^dIntroduction to only part of the country. ^eIntroduction to National Immunization Program but initially only funds available to vaccinate an estimated 700 000 infants from the poorest communities.

may be factor in delaying policy decisions for rotavirus vaccine introduction in the region, and have certainly impacted cost effectiveness analyses. However, it is worth noting that similar moderate levels of vaccine efficacy have not slowed vaccine introduction in the African region.

Economic Evaluations and Vaccine Price

Economic evaluations should typically be performed prior to a decision being made to introduce a new vaccine. The typical economic evaluation will take a number

factors into consideration including: direct and indirect costs; averted illnesses, averted deaths, disability-adjusted life years (DALYs) and quality-adjusted life years (QALYs) averted/gained, avoided medical and indirect costs.³¹ The main drivers of the model are typically the price of the vaccine and number of deaths and hospitalizations averted.

The outcome of this type of analysis can be shown on a cost-effectiveness plane which has 4 quadrants (Fig. 1). Typically most analyses fall in the top right quadrant where the intervention (vaccination) is more costly than the existing intervention

(no vaccination and hospitalizations/deaths from rotavirus) but more effective (prevents hospitalizations/deaths from rotavirus). If the intervention is a lot more costly, but only a little bit more effective, it will be deemed not cost-effective i.e., to left of the incremental cost-effective ratio (ICER) line (Price A, Fig. 1). Conversely if it is a little more costly but a lot more effective it will be deemed cost-effective i.e., to the right of the ICER line (Price B, Fig. 1). Very occasionally decision makers may opt for an intervention that falls in the bottom left quadrant i.e., the intervention is less costly than the existing intervention

but also less effective. This would be a rational decision if the intervention is a lot less costly but only a little bit less effective since it might be possible to cover a much greater proportion of the population with the intervention i.e., falls to the right of the ICER line. Ideally, the analysis will fall in the bottom right quadrant. Here the intervention is less costly than the existing intervention but more effective i.e., Government would save money and make its population more healthy (Price C, Fig. 1). When a decision is made not to adopt such an intervention, it is important to have clear and evidenced-based reasons why the intervention cannot be introduced.

However for this type of analysis to work optimally the cost of the intervention (primarily vaccine price) needs to be very precise since this is a key driver of the model. There are a number of published economic evaluations conducted on rotavirus vaccines that have used the catalog or private sector list price, with or without an assumed discount, for the analysis, which have then concluded that rotavirus immunization is likely to be not cost-effective at this price.³² Although sensitivity analyses are undertaken as part of economic evaluations to show the impact of decreasing or increasing the vaccine price, the conclusion that the vaccine will not be cost-effective at current market price, is likely to be an important influencer for decision makers. If economic modelers use the private sector list price, or a closely related price, decision-makers are likely to conclude that rotavirus vaccine is not cost-effective (Price A, Fig. 1). Although the likely tender price for public health use of a vaccine in a National Immunization Program (NIP) (i.e., bulk purchase contract for several years) will typically be very much less than the private sector price (Price B and C, Fig. 1), this lower price cannot be known until after the vaccine has been recommended for use and tendering process completed. This “catch-22” may result in decision-makers deferring vaccine introduction decisions. One way to solve this problem is to ensure that the tender price or purchase price is known prior to conducting the economic analysis and before an informed decision

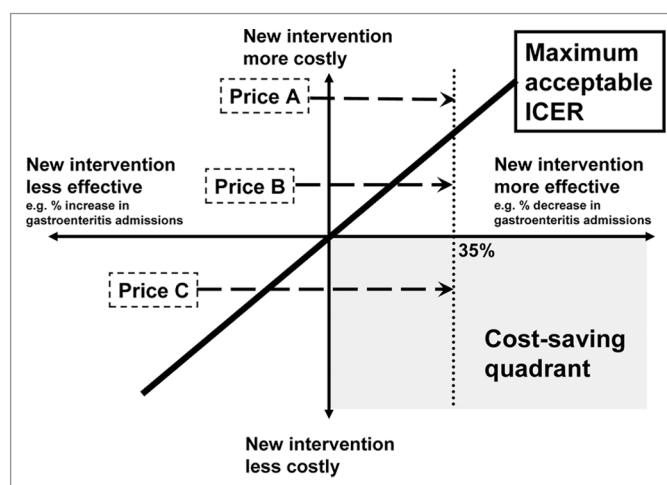


Figure 1. Cost-effectiveness plane showing how vaccine price typically drives the economic model and can easily change the conclusion that introducing a new vaccine will be cost-ineffective (price A), cost-effective (price B) or cost-saving (price C). Often the private sector list or catalog price lies in the region of Price A, whereas an eventual tender or agreed price for use of a vaccine in a National Immunization Program lies between Price B and C. Rotavirus vaccine introductions in early-adopter countries have resulted in a 35% decrease in all-cause gastroenteritis hospitalizations in children below 2 y of age.¹⁸

is made whether or not to introduce the vaccine into the NIP.

In addition it should be noted that although immunization are widely recognized as one of the most cost-effective of all health interventions,³³ it is also likely that their economic benefits have been underestimated since wider economic benefits are not considered in traditional economic evaluations.³⁴

National Immunization Technical Advisory Groups

Ideally decisions on public health policy should be transparent, be based on the best available evidence and be free from external interests—political, commercial, special interest. Given the increasing complexity of immunization programs and the high cost of new vaccines, WHO SAGE recommended in 2009 that, as part of the process of ensuring evidence-based decision-making at the country level, it was a priority for countries to establish and/or strengthen their national immunization technical advisory committees (NITAGs). NITAGs help health authorities formulate immunization policies according to the specific needs of their country, while

taking into account the regional and international context.³⁵ In 2008 the Bill and Melinda Gates Foundation funded an initiative to establish or strengthen independent NITAGs. Detailed descriptions of the experiences and processes of 15 well established NITAGs from all regions of the world highlighted considerable differences between committees including their legal basis, size and scope of committee membership, scope of work, role of the Ministry of Health on the committee, existence of conflict of interest policies, and ultimate role in the decision-making process.³⁶ Nevertheless, NITAGs are recognized as a crucial component for national decision-making for new vaccines, and should be developed nationally as a priority.

Decision-Making and NITAGs in Some Early-Adopter Countries

The United States and Australia were both early adopters of rotavirus vaccines and both have well established NITAGs.^{37,38} The United States was the first country to recommend the universal use of both Rotashield® (in 1998) and RotaTeq® (in 2006). The Advisory Committee on Immunization Practices (ACIP) provides

Table 2. Rotavirus disease burden reported from sites participating in the Asian Rotavirus Surveillance Network

Sites	Surveillance period	Proportion of diarrhea-related hospitalizations under the age of 5 years positive for rotavirus
Bangladesh ^c	2005–7	33
Cambodia ^c	2005–7	56
China ^a	2001–4	50
China ^b	2005–7	48
Fiji ^c	2005–7	39
Hong Kong ^a	2001–4	30
India ^b	2005–7	39
Indonesia ^{b,d}	2005–7	60
Japan ^a	2001–4	58
Kyrgyzstan ^c	2005–7	26
Lao ^c	2005–7	54
Mongolia ^b	2005–7	40
Myanmar ^a	2001–4	53
Myanmar ^c	2005–7	55
Nepal ^b	2005–7	33
Pakistan ^{c,e}	2005–7	17
Philippines ^b	2005–7	31
South Korea ^c	2005–7	22
Sri Lanka ^b	2005–7	24
Taiwan ^a	2001–4	43
Taiwan ^c	2005–7	25
Thailand ^a	2001–4	43
Uzbekistan ^b	2005–7	30
Vietnam ^a	2001–4	55
Vietnam ^c	2005–7	52

^aData from J Infect Dis. 2005;192(suppl 1). ^bData from J Infect Dis. 2009; 200 (suppl 1). ^cData from Vaccine 2009; 27 (suppl 5). ^dAdmissions under 3 y of age. ^eCommunity study.

advice and guidance to the Secretary of the United States Department of Health and Human Services, the Director of the United States Centers for Disease Control and Prevention and other decision makers regarding the most appropriate selection of vaccines and related agents for effective prevention and control of vaccine-preventable diseases in the civilian population.³⁹ ACIP's recommendations include consideration of population-based studies such as efficacy, cost benefit, and risk benefit analyses. ACIP also establishes a list of vaccines for administration to children and adolescents eligible to receive vaccines through the federal Vaccines for

Children Program and this list is used for the purchase, delivery, and administration of pediatric vaccines under this program. Currently the private sector price for RotaTeq[®] (3 dose) and Rotarix[®] (2 dose) per course is approximately \$226 and \$213 respectively, which is somewhat higher than the \$192 and \$184 paid for the same vaccines by the Vaccines for Children Program (Table 3).⁴⁰

The Australian Technical Advisory Group on Immunization (ATAGI) is tasked to provide technical advice to the Minister for Health and Aging on the medical administration of vaccines available in Australia, including those in the NIP.³⁷

The group also advises the Pharmaceutical Benefits Advisory Committee (PBAC) on the strength of evidence relating to existing, new and emerging vaccines in relation to their effectiveness and use in Australian populations. The ATAGI provides advice to both PBAC and to the submitting company about the public health and technical factors considered to be important to the public interest. However cost-effectiveness assessments are the sole responsibility of PBAC. Once the vaccine is supported by ATAGI, the vaccine manufacturer will then submit an application to PBAC and request that the vaccine be considered either for an NIP listing (free to eligible people) or a listing that requires a co-payment under the Pharmaceutical Benefits Scheme. PBAC's Economic Sub-committee will review and interpret the company's submission and economic analyses. PBAC will then provide a recommendation to Government on whether or not to fund the vaccine and on what basis. In contrast to the United States, the price that the Australian government pays for a vaccine included in the NIP is not in the public domain.

Apart from some small island states with strong historical links to Australia and the United States, the Philippines was the first Asian country to announce plans to introduce rotavirus vaccine (Table 1). This announcement was possible following a recommendation by the Ministry of Health and a decision by the Ministry of Finance to identify a specific sum of money to support the program. At the time of the announcement it was unknown which vaccine (or how many doses) would be used since the tendering process had not occurred - the lower the tender price, the more children could be vaccinated. In July 2012, six months after the announcement, the program was started with the Minister of Health reporting that during the first year 700 000 infants from the poorest communities would receive rotavirus vaccine i.e., approximately 28% of the 2.5 million birth cohort.

In contrast to Asia, the Americas were quick to use rotavirus vaccines, with 8 of the 12 early adopters (2006/2007) of rotavirus vaccines being situated in the Pan American Health Organization (PAHO)

region (Table 1). Haiti, the last remaining GAVI-eligible country in the PAHO region yet to introduce rotavirus vaccine into its NIP, did so in May 2013. The early introduction of rotavirus vaccines into NIPs in the Americas can be explained in part by several factors, including good burden of disease data, and the fact that the initial rotavirus vaccine studies were predominantly conducted in the Americas as highlighted in WHO's 2007 position paper.³ In addition, PAHO's Revolving Fund played an important role in decision-making and expediting rotavirus vaccine introduction in the region.^{41–43}

Pricing Options for Asia

Revolving fund for vaccine procurement

PAHO countries pay per rotavirus vaccine course (2 or 3 doses) \$13 for Rotarix[®] and \$15.45 for RotaTeq[®].⁴⁴ This price is in the public domain and provides the decision making process a precise estimate of vaccine cost as a result of PAHO's Revolving Fund for Vaccine Procurement. The Revolving Fund is a mechanism to facilitate the bulk purchase of vaccines, syringes, cold chain equipment and related supplies.^{41,43} Taking advantage of economies of scale, the Revolving Fund secures vaccines—prequalified under WHO standards of safety and effectiveness—for member states at affordable prices. By purchasing through the Revolving Fund instead of directly from producers, countries can make significant savings on the purchase price. Founded on the principle of equity, PAHO's Revolving Fund enables all participating member states to have access to the same products, offered at the lowest price, which is the same regardless of the country's size or economic situation. Member states all contribute three percent of each net purchase price to a common fund which is used as working capital. Member states in need can take out lines of credit to purchase their vaccines, repaying within 60 d of vaccine receipt. The Revolving Fund also handles key processes like planning, demand estimates, price negotiations, purchase orders, supply coordination, shipment monitoring and billing. As a

Table 3. Examples of prices per course in US\$ for Rotarix[®] and RotaTeq[®]

Country / Region	Vaccine	Price (US \$ per course)
United States of America ⁴⁰		
	RotaTeq [®]	US \$192 (CDC) US \$226 (PVT)
	Rotarix [®]	US \$184 (CDC) US \$213 (PVT)
United Kingdom ^a	Rotarix [®]	US \$45 Approximate estimate based on publicly announced cost of program divided by birth cohort
PAHO ⁴⁴		
	RotaTeq [®]	US \$15.45
	Rotarix [®]	US \$13
GAVI	Rotarix [®]	US \$ 5
GAVI-eligible countries	Rotarix [®]	US \$ 0.30–\$ 0.60 The is the subsidized co-pay price that countries pay during the time that they receive GAVI support ^b
Australia	RotaTeq [®] or Rotarix [®]	Not in public domain
Philippines	Rotarix [®]	Not in public domain

^aVaccine to be introduced July 2013 after previously considered cost-ineffective applying a 15% discount (US \$125 per course) to the catalog price of US \$148 per course for Rotarix[®].³² ^bThis can be a major concern for decision-makers in countries that “graduate” for GAVI-eligibility and have to purchase vaccine through some other mechanism.

result, Latin American countries have had continuous access to safe and effective vaccines at low, stable prices for over 30 y. This assists national governments with budget planning, and fosters sustainable immunization programs. Today, the vast majority of vaccines being used in Latin America for some 44 million people were acquired through the Revolving Fund. However PAHO's Revolving Fund does not have a mechanism to tier the pricing of vaccine between its more or less affluent members.

Tiered pricing

Industry, in particular GlaxoSmithKline Biologicals, indicates that it is willing to enter into tiered pricing agreements with individual governments.⁴⁵ However the prices agreed between the company and individual countries are generally not in the public domain to guide decision makers in other countries. Although an attractive concept for some countries, such one-to-one negotiations may be in conflict with

the legal requirements of the tendering process of other countries.

Separating technical decisions from economic evaluations

The ATAGI/PBAC mechanism as described above was introduced in 2005 by the Australian government to bring vaccine funding applications into the same transparent and predictable mechanism that had been used successfully for drugs.³⁷ However in contrast to PAHO's Revolving Fund the price paid by Australia for rotavirus vaccines is not publicly released. This mechanism allows Australia to enter into a process with industry, to obtain a price that is acceptable to both. However smaller countries with less capacity may have difficulty managing such a process and are likely to prefer a regional tendering process like PAHO's Revolving Fund.

UNICEF hybrid procurement strategy

Recently UNICEF presented a strategy for vaccine procurement for middle-income countries that would include providing

industry with demand forecasts, providing countries with information on products and availability; pooling procurement and establishing reference pricing.⁴⁶

Conclusions

Although decisions on vaccine introduction are complex and impossible to fully dissect for each country,²⁴ it is clear that current understanding of “local data on disease burden” and “cost benefit of the vaccine” may not reliably inform decision-makers on new vaccine introduction. In particular, concerns about vaccines being too costly are often made without consideration of optional funding strategies by the scientific community and may not reflect potential tender or negotiated prices. This can impact an informed decision-making process for countries, and remove a sense of urgency for new vaccine introduction. The ARSN does pre-empt a claim of “lack of local data on disease burden” for many countries in the Asian Region, but it is hard to address concerns about vaccine price being too costly when the vaccine price cannot be known ahead of a tendering process, and the prices in the private market are very high.

What pricing solutions could help Asian policy-makers decide whether rotavirus vaccine is a “good buy” for them? An Asian or ASEAN revolving fund is clearly one option. However to set up such a fund would be challenging and requires considerable political will and international coordination with ASEAN Health and Finance Ministers. Regional WHO offices could take the lead to encourage the establishment of such a fund, but a SAGE recommendation to this effect would probably be required. In addition preliminary seed funding would be needed. Individual countries could try to establish funding mechanisms similar to Australia’s ATAGI/PBAC mechanism where a recommendation on vaccine use is separated from a decision as to whether the government will pay for the vaccines. However for some countries this is not feasible where a government recommendation for vaccine use is considered synonymous to the government agreeing to pay for the vaccine prior to the tendering process. Finally one-to-one

discussion with industry may be needed to try to gain an advantageous tiered pricing agreement. But for those governments facing difficult trade-off decisions, or that wish to delay the decision, the lack of good local economic evaluations based on corrected pricing estimates remains a cry of despair “the vaccine price is too high!”

Disclosure of Potential Conflicts of Interest

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Centers for Disease Control and Prevention (CDC).

Competing Interests

EASN has participated in a vaccine studies funded by Baxter, GlaxoSmith-Kline, MedImmune, and Wyeth, has received funding to conduct disease surveillance studies from Merck and Pfizer, and lecture fees and travel support from GlaxoSmithKline, Merck, Intercell, and Pfizer. The other authors have declared that no competing interests exist

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